I. THE STRUCTURES OF CARTHAMOIDINE AND RETRONECINE

II. RESTRICTED ROTATION IN ARYLAMINES

BY

RICHARD FIFIELD PHILLIPS

A.B., Amherst College, 1939

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY IN THE GRADUATE SCHOOL OF THE UNIVERSITY OF ILLINOIS, 1942

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Part I.

THE STRUCTURES OF CARTHAMOIDINE AND RETRONECINE

Introduction

The alkaloids from *Senecio, Crotalaria, Heliotropium, Trichodesma, Erechtites,* and *Trachelanthus* promise to be by far the largest of any single known class. These alkaloids are esters of acids containing eight or ten carbon atoms and one of several related amino alcohols. The base which occurs most frequently is retronecine, a derivative of 1-methylpyrrolizidine, possessing two hydroxyl groups and one ethylenic linkage. One of the hydroxyl groups is activated by the double bond so that it is readily hydrogenolyzed.

Discussion and Experimental

Adams and Rogers[1] postulated retronecine to be 1,7-dihydroxy-1-methyl-1,2,7,8-tetrahydro-4,3-pyrrolopyrrole (see The Ring Index[2]).

Two attempts were made to synthesize 1-hydroxy-1-methylpyrrolizidine which would be identical with retronecanol, a reduction product of retronecine.

potassium pyrrole + β-cyanoethyl *p*-toluenesulfonate→

1-β-cyanoethylpyrrole $\xrightarrow{\text{HCl followed by hydrolysis}}$

1-keto-1,2-dihydro-4,3-pyrrolopyrrole $\xrightarrow{CH_3MgI}$

1-hydroxy-1-methyl-1,2-dihydro-4 3-pyrrolopyrrole $\xrightarrow{H_2}$

1-hydroxy-1-methylpyrrolizidine.

The Grignard reaction did not give the desired product. The second proposed synthesis follows:

proline ethyl ester + ethyl acrylate $\xrightarrow{\text{metallic potassium}}$ ethyl β-N-(2-carbethoxypyrrolidyl)-propionate $\dashrightarrow$ 1-ketopyrrolizidine $\xrightarrow{CH_3MgI}$ 1-hydroxy-1-methylpyrrolizidine.

The ketopyrrolizidine was a very unstable substance. The subsequent Grignard reaction gave negative results. The work on this second synthesis was done in collaboration with Dr. Marvin Carmack, formerly of this laboratory.

Recent evidence strongly favors a different structure for retronecine, 1-hydroxymethylene-7-hydroxy-5,6,7,8-tetrahydro-4,3-pyrrolopyrrole.[3]

Alkaloids were extracted from *Senecio Riddellii, S. eremophilus, S. Douglasii,* and *S. carthamoides.* The latter three are new. Riddelliine had been previously reported by Manske.[4] Saponification of carthamoidine, $C_{18}H_{23}O_5N$, the alkaloid from *S. carthamoides,* yielded retronecine and carthamoidinecic acid, $C_{10}H_{14}O_5$. On hydrogenation of the alkaloid three moles of hydrogen were absorbed; saponification of the amorphous hydrogenation product gave retronecanol and a non-crystalline acid. Carthamoidinecic acid is dibasic, contains one double bond and one hydroxyl group, and therefore must be monocyclic.

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Part II.

RESTRICTED ROTATION IN ARYLAMINES

Introduction

Many instances of molecular asymmetry and, therefore, optical activity occur because free rotation about a valence bond is prevented by steric hindrance. Mills[1] resolved aromatic

amines in which the only asymmetric center was due to restricted rotation between the amine nitrogen and the aromatic carbon to which it was attached. Adams and Dankert[2] and Adams and Stewart[3] studied several substituted N-succinyl-N-alkylanilines in which the *ortho*-groups and the N-alkyl substituent were varied.

Discussion and Experimental

N-Phthalyl-N-methyl-3-bromomesidine and N-maleyl-N-methyl-3-bromomesidine were prepared by the acylation of N-methyl-3-bromomesidine with phthalic and maleic anhydrides respectively.

The resolution of the phthalyl derivative was carried out through the separation of the diastereoisomeric salts of *d*-pseudoephedrine by fractional crystallization. Only a small quantity of the pure less-soluble salt was obtained. Decomposition of the salt gave the pure *d*-acid which had a specific rotation of + 56° in 95% ethanol. The more-soluble salt could not be purified; it yielded a *l*-acid having specific rotation -13° in 95% ethanol.

The maleyl derivative, in contrast to the phthalyl and succinyl compounds, very readily formed nicely crystalline salts with common alkaloids. The resolution was effected through crystallization of the brucine salt. Difficulty was encountered in regenerating the optically active acid from the salt in crystalline form, but very recently the acid has crystallized.

In order to study a compound which would have two asymmetric centers each due to restricted rotation about a C-N bond, the following diamides were prepared: N,N′-dimethyl-N,N′-dimesitylfumaramide, N,N′-dimethyl-N,N′-dimesitylsuccinamide, and N,N′-dimethyl-N,N′-di-(3-bromomesityl)-fumaramide Only one of the two expected diastereoisomers of the last could be isolated. Similarly, attempts to introduce two points of asymmetry in the succinamide by monosubstitution of each ring and to obtain the two expected diastereoisomers have been unsuccessful.

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VITA

The writer was born in Worcester, Massachusetts, on July 4, 1917. He received his elementary education in the public schools of that city. After graduation from North High School in June, 1935, he received a scholarship at Amherst College which he held until June, 1939, when he received the degree of Bachelor of Arts. During the year 1939-1940 he held the Forris Jewett Moore Fellowship from Amherst College for graduate study at the University of Illinois. He was a University Fellow during the year 1940-1941 and the Du Pont Fellow for the year 1941-1942.

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